REMARKS

Claims 3-12 and 14-29 are currently pending. Claims 1,2, and 13 have been canceled and claims 21-29 are newly presented. Claims 3-6,8,11,12,14, and 15 have been amended. Applicants respectfully submit that the amendments to the claims are supported in the specification as originally filed, thus no new matter is presented thereby. Entry of the amendments is respectfully requested.

Claims 2-4, 11-13, and 19 have been objected to as being of improper dependent form for failing to limit the independent claim. In particular, the Examiner states that claims 2 and 3 are unclear as to how the emitted doses further limit the base claim. The Examiner further states that the emitted dose is an inherent characteristic of the method. Similarly regarding claim 4, the Examiner states that the fine particle fraction (FPF) is an inherent characteristic of the base method.

Claim 2 has been canceled and incorporated into new independent claim 21. Claim 3 has been amended to recite a range of emitted dose from 80-100%. Claim 4 has been amended to recite the definition for the acronym "$FPF_{4+F}$" as defined at page 6, lines 26-30. Applicants respectfully submit that these limitations clearly recite the superior aerosolization properties of the powders due to particle engineering of the present invention and must be considered.

Claims 1-4 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claim 1 has been replaced with claim 21, which recites that "the emitted dose of said composition from said passive dry powder inhaler is at least 60% w/w and is substantially independent over an inhalation flow rate of 20-90 l/min and device resistance of 0.04-$0.20(cmH_2O)^{1/2}$ /L $min^{-1}$" (emphasis added). Applicants respectfully submit that the rejection under 35 U.S.C. 112, second paragraph has been overcome and should be withdrawn.

The Examiner has rejected the claim as the term "substantially" is a relative term which renders the claim indefinite. As seen in the specification, a recognized drawback of the prior art is that performance of many dry powder inhalers is dependent upon the patient's inspiratory effort. (See page 2, lines 12-19 of the present specification and Schultz et al.: page 1, lines 21-23). In contrast to prior efforts to address this problem through device design, the present invention relies upon a particle engineering approach to overcome such issues, as indicated in the

specification, for example at page 3, lines 19-26, page 7, lines 5-10, 17-25. The Examples give further guidance to one of ordinary skill as to the substantially independent emitted dose achieved over a variety of inspiratory flow rates and device resistances.

For example, Table 1 of Example 1 shows the emitted doses achieved from aerosolization via a number of devices of differing resistances at various inspiratory flow rates. As seen in the table, the emitted doses were in a narrow range. Table 2 of Example 2 shows deposition data where formulations of the present invention resulted in substantially the same deposition whereas prior art formulations varied by almost a factor of two. Tables 4 and 6 also show fine particle fractions achieved via aerosolization via two different devices at various flow rates, also giving guidance to one of ordinary skill. Thus, applicants respectfully submit that the claim language "wherein the emitted dose of said composition from said passive dry powder inhaler is at least 50% w/w and is substantially independent over an inhalation flow rate of 20-90 l/min and device resistance of 0.04-0.20$(cmH_2O)^{1/2}$ /L $min^{-1}$" is definite in view of the guidance given in the specification as filed. See M.P.E.P 2173.05(b)(D).

Claims 1-20 have been rejected under 35 U.S.C. 103 as being unpatentable over Schultz et al. in view of Van Oort et al. and Edwards et al. Claim 1 has been replaced by claim 21 in order to address the indefiniteness issues raised by the Examiner as discussed above. It is respectfully submitted that the proposed rejection under 35 U.S.C. 103 is improper and should be withdrawn for the reasons that follow.

Each of the independent claims recites administering the composition from a passive dry powder inhaler. This term is clearly defined in the specification as a device which relies upon the patient's inspiratory effort to disperse and aerosolize a formulation contained within the device and does not include devices which include a means for providing energy to disperse and aerosolize the drug formulation, such as pressurized gas and vibrating or rotating elements (page 6, lines 18-22).

The rejection as set forth by the Examiner proposes modifying the methods of Schultz et al. and Van Oort et al. by employing a dry powder as disclosed in Edwards et al. Such a proposed modification fails to disclose or suggest the claimed invention. The claims require administering the composition from a passive dry powder inhaler as discussed above. The device of Schultz et al. is an active inhaler, wherein a motorized impeller is used to aerosolize and disperse the powder formulation.

For the benefit of the Examiner, a copy of PCT WO 94/08552, corresponding to PCT/US93/09751 incorporated by reference in Schultz et al. (page 2, line 27-29) is enclosed herein. As seen at Schultz et al. (page 2, lines 27-29), the sole device utilized therein is the SPIROS device described in WO 94/08552. This device utilizes an impeller disposed within a mixing chamber, which is spun by a high speed motor (See the Abstract). As such, the teachings of Schultz are limited to the use of active dry powder inhalers.

To arrive at the claimed invention, one of ordinary skill would have to modify the device disclosed in Schultz et al. in such a way as to destroy the operability of that device. Thus, the combination as proposed by the Examiner fails to render the claimed invention obvious and should be withdrawn.

Lastly, newly presented claims recite administering the composition in a single breath to achieve an emitted dose of at least 80% w/w (claim 28) and a fine particle fraction of particles less than 3.3 microns of at least 35% w/w (claim 29). Applicants respectfully submit that the prior art fails to disclose or suggest the subject matter as presented in these new claims.

## CONCLUSION

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made"**

Applicants believe that all the pending claims are presently in condition for allowance. However, the Examiner is invited to telephone the undersigned attorney at the number below if it is believed that this will expedite prosecution of the present application.

Respectfully submitted,

Dated: 3/5/02

By: _____

Michael J. Rafa.
Registration No. 38,740
Attorney of Record
(650) 631-5053

MARKED UP SET

Claims 1 and 2 have been canceled.

3. A method according to claim 21 comprising an emitted dose of [at least] 80 - 100% w/w.

4. A method according to claim 21 comprising a [$FPF_{4+F}$] fraction of particles depositing on stage 4 and the filter of a multistage liquid impinger of at least 60% w/w.

5. A method according to claim 21 wherein the lipid comprises a phospholipid selected from the group consisting of dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, diarachidoylphosphatidylcholine dibehenoylphosphatidylcholine, diphosphatidyl glycerol, short-chain phosphatidylcholines, long-chain saturated phosphatidylethanolamines, long-chain saturated phosphatidylserines, long-chain saturated phosphatidylglycerols, and long-chain saturated phosphatidylinositols.

6. A method according to claim 21 wherein the inhaler comprises a resistance of less than 0.60 $(cmH_2O)^{1/2}$ /L $min^{-1}$.

8. A method of claim 21 wherein the inhalation flow rate is less than about 90 L/min.

11. A method of claim 21 wherein the lung deposition is greater than 25% w/w of the nominal dose.

12. A method according to claim 21 wherein the lung deposition is about [greater than] 30 - 60% w/w of the nominal dose.

Claim 13 has been canceled.

14. A method according to claim 21 wherein the drug is selected from the group consisting of budesonide, tobramycin sulfate, leuprolide acetate, Amphotericin B, and [PTH] parathyroid hormone.

15. A method of claim 21 wherein the powder comprises hollow porous microparticles.

Claims 21-29 are new.